

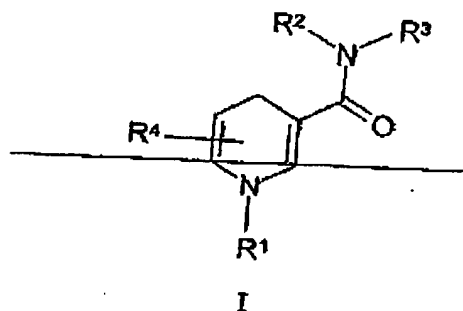
U.S.S.N. 09/445,865

Filed: February 11, 2000

## AMENDMENT AND RESPONSE TO OFFICE ACTION

## In the Claims

29. (Twice Amended) A method of treating a human patient with a target cell to be destroyed wherein the target cell expresses NQO2 the method comprising administering to the patient a prodrug which is converted to a cytotoxic drug by the action of NQO2 and an analogue of nicotinamide riboside (reduced) (NRH) having formula I:



which can pass reducing equivalents to NQO2, wherein the prodrug is CB 1954, and wherein R<sup>1</sup> is selected from the group consisting of: substituted alkyl, including substitution by CONH<sub>2</sub>, OH, halogen, CN and COOH; alkyl; aryl; substituted aryl; CONR<sup>a</sup>R<sup>b</sup>, where R<sup>a</sup> and R<sup>b</sup> are independently H, alkyl, or substituted alkyl, and R<sup>2</sup> and R<sup>3</sup> are independently H, alkyl, or substituted alkyl and R<sup>4</sup> is any of H, alkyl, substituted alkyl, halogen, CN, COOH, CONH<sub>2</sub> or OH.

31. (Amended) The method of claim 29 wherein the analogue of NRH is able to permeate the target cell membrane.

32. (Amended) The method of claim 29 wherein the target cell is a tumour.

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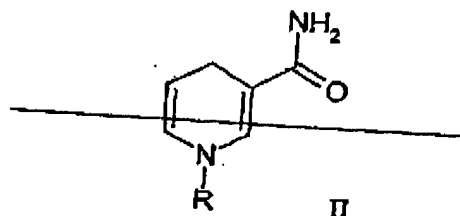
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33. (Three times amended) The method of claim 29, the method further comprising determining, before administering the prodrug an and analogue of NRH, whether the target cell to be treated expresses NQO2.

40. The method of claim 29 wherein the patient has cancer.

41. (amended) A The method of ~~claim 29~~, treating a human patient with a target cell to be destroyed wherein the target cell expresses NQO2 the method comprising administering to the patient ~~wherein the analogue of NRH is 1-(carboxamidomethyl)-dihydronicotinamide.~~

42. (New) The method of claim 29, wherein the analogue of NRH has formula II:



wherein R is selected from the group consisting of: substituted alkyl, including substitution by CONH<sub>2</sub>, OH, halogen, CN and COOH; and alkyl.

43. (unamended) The method of claim 29 wherein the alkyl group is C<sub>1</sub> to C<sub>6</sub> alkyl.

44. (unamended) The method of claim 42 wherein R is selected from the group consisting of: -CH<sub>2</sub>CONH<sub>2</sub>; -CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>SO<sub>3</sub><sup>-</sup>; -CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>; -CH(CH<sub>3</sub>)<sub>2</sub>; -CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>OH; -CH<sub>2</sub>CH<sub>2</sub>OH; CH<sub>2</sub>CH<sub>2</sub>COOH; -CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>; -CH<sub>3</sub>; -CH<sub>2</sub>CH<sub>3</sub>; -CH<sub>2</sub>CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>.